Sub. File 19

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dicamba. Case 0065. Confined Rotational Crop Study. MRID 41972001. CBRS 12947. DP Barcode:D197629.

FROM: Leung Cheng, Chemist
Special Review Section I
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THROUGH: Andrew R. Rathman, Section Head
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TO: Jane Mitchell, CRM
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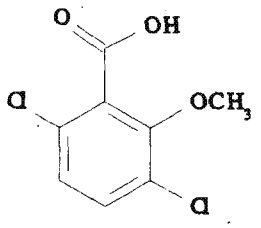
Attached please find a review of confined rotational crop study submitted by Sandoz Agro Inc in response to the Dicamba (SRR) Reregistration Standard (6/30/89). These data were reviewed by Dynamac Corporation under the supervision of CBRS, HED. This information has undergone secondary review in CBRS and is consistent with Agency policies.

The submitted study is unacceptable and a new study is required. Upgrading of the study is not feasible because it was completed in 1988. The registrant should consult "Guidance on How to Conduct Studies on Rotational Crops", E. Zager and D. Edwards, 2/23/93.

Attachment - Dynamac review of Registrant's Response to Residue Chemistry Data Requirements

cc(with Attachment):Circ, SF, RF, Reg Std File, Cheng
RDI:ARRathman:2/12/96:RBPerfetti:2/13/96:EZager:2/15/96
7509C:CBRS:LCheng:CM#2:RM804D:2/2/96:■05:DICAMBA\ROTATION

DICAMBA



Shaughnessy No. 029801; Case No. 0065

(CBRS No.12947; DP Barcode D197629)

Task 4

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

Sandoz Crop Protection Corporation has submitted a confined rotational crop study (1991; MRID 41972001) which is evaluated in this document for adequacy in fulfilling the residue chemistry reregistration requirements under Guideline Reference No. 165-1.

The qualitative nature of the residue in plants is adequately understood. The residues of concern in/on plant commodities (except in/on asparagus, soybeans, and soybean forage and hay) are dicamba and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid. The residues of concern in/on asparagus, soybeans, and soybean forage and hay are dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid. The qualitative nature of the residue in animals is not adequately understood; the requirements for metabolism studies on ruminants and poultry remain outstanding.

Tolerances for residues in/on various plant (excluding soybeans, soybean forage and soybean hay) and processed food/feed commodities are currently expressed in terms of the combined residues of dicamba (3,6-dichloro-*o*-anisic acid) and its metabolite 3,6-dichloro-5-hydroxy-*o*-anisic acid [40 CFR §180.227(a), §185.1800, and §186.1800]. Tolerances for residues in/on soybeans, soybean forage and soybean hay, and in animal commodities are expressed in terms of the combined residues of dicamba and its metabolite 3,6-dichloro-2-hydroxybenzoic acid [40 CFR §180.227(b)].

The Pesticide Analytical Manual (PAM) Vol. II lists Method I and II, GC methods with electron capture detection (GC/ECD) for the enforcement of tolerances on dicamba and its metabolite 5-hydroxy dicamba in/on plant commodities and milk. There are no Codex MRLs for residues of dicamba; therefore, issues of compatibility between U.S. tolerances and Codex MRLs do not exist.

CONCLUSIONS AND RECOMMENDATIONS

1. The submitted confined rotational crop study is inadequate to satisfy the 165-1 guideline requirements because the test substance, uniformly ring-labeled [^{14}C]dicamba acid, was applied at only 0.5 lb ae/A (0.67x the maximum registered dicamba label rate for annual crops). The possibility of obtaining rotational crop commodity samples with sufficient radioactive residues (e.g., at the 131- and 369-day plantback interval) may have been compromised as a result of the <1x application rate. Furthermore, the reported results of the characterization and identification of radioactive residues, using samples from the 32-day plantback interval, are inconclusive since details and quantitative raw data (e.g., material balance to account for the radioactivity in extractable and non-extractable fractions as well as sample chromatograms) were not provided. Upgrading the study by conducting further analyses on stored samples is not feasible because the study was initiated in 1986. A new confined rotational crop study must be conducted.

2a. Data in the present study indicated that radioactive residues in/on rotated crops following a 0.67x application rate and 32-day plantback interval were: 0.213 ppm in mustard greens, 0.0325 ppm in wheat forage, and 0.0153 ppm in turnips. Radioactive residues were <0.01 ppm in/on rotated crops from the 131- and 369-day plantback intervals.

2b. Attempts were made to characterize and identify radioactive residues in/on commodities from the 32-day plantback interval. The registrant reported that dicamba, 3,6-dichlorosalicylic acid, and 5-hydroxy dicamba were quantified by GC/ECD at levels <0.01 ppm. These findings are not supported by adequate quantitative raw data.

3. The need for limited/extensive rotational crop studies (Guideline Reference No. 165-2) and possible label plantback restrictions will be determined when an acceptable confined rotational crop study has been submitted and evaluated. The registrant should consult "Guidance on How to Conduct Studies on Rotational Crops", E. Zager and D. Edwards, 2/23/93.

DETAILED CONSIDERATIONS

Registered Use Patterns

A REFS search conducted 4/27/94 identified numerous dicamba end-use products and formulations registered to Sandoz. A summary of dicamba use patterns on annual food/feed crops is presented in Table 1. For purposes of this evaluation, the maximum application rate is 0.75 lb acid equivalent (ae) per acre. These various formulations listed in Table 1 may be made preplant, preemergence, and postemergence as broadcast applications using ground (3-50 gal/A) or aerial (1-10 gal/A) equipment. The labels do not specify plantback intervals when dicamba is applied on annual food/feed crops.

Table 1. Summary of dicamba use patterns on annual food/feed crops.

Crop	Formulation (EPA Reg. No.)	Mode of Application	Maximum Application Rates
Barley	2 lb/gal SC/L sodium salt (55947-28)	Postemergence	0.094-0.125 lb ae/A for spring and fall seeding
	4 lb/gal SC/L potassium salt (55947-38)		0.125 lb ae/A for fall seeding
	3 lb/gal SC/L isopropylamine salt (55947-47)		0.3 lb ae/A
Corn	2 lb/gal SC/L sodium salt (55947-28)	Preplant, pre- and postemergence	0.25 lb ae/A for preplant or preemergence application; 0.5 lb ae/A for postemergence application; A maximum seasonal rate of 0.75 ae/A
	4 lb/gal SC/L potassium salt (55947-38)		0.5 lb ae/A
	1.1 lb/gal FlC potassium salt (55947-39)		0.75 lb ae/A [alone or sequential with 4 lb/gal SC/L potassium salt]
	4 lb/gal SC/L diglycoamine salt (55947-46)		0.5 lb ae/A
Oats	2 lb/gal SC/L sodium salt (55947-28)	Postemergence	0.125 lb ae/A [spring and fall seeded]
	4 lb/gal SC/L potassium salt (55947-38)		0.125 lb ae/A for spring and fall seeding
	3 lb/gal SC/L isopropylamine salt (55947-47)		0.3 lb ae/A
Sorghum	4 lb/gal SC/L potassium salt (55947-38)	Postemergence	0.25 lb ae/A
	1.1 lb/gal FlC potassium salt (55947-39)		0.275 lb ae/A
	3 lb/gal SC/L isopropylamine salt (55947-47)		0.375 lb ae/A
Wheat	1.25 lb/gal SC/L dimethylamine salt (55947-7)	Postemergence	0.125-0.188 lb ae/A for spring and fall seeding
	1 lb/gal SC/L dimethylamine salt (55947-24)		0.125 lb ae/A for and spring and fall seeding
	2 lb/gal SC/L sodium salt (55947-28)		0.125 lb ae/A for spring and fall seeding
	4 lb/gal SC/L potassium salt (55947-38)		0.125 lb ae/A for spring and fall seeding
	3 lb/gal SC/L isopropylamine salt (55947-47)		0.3 lb ae/A

In-Life Phase

The in-life phase of the study was conducted by North Carolina State University Central Research Station (Clayton, NC). Uniformly ring-labeled [^{14}C]dicamba acid (radiochemical purity 98%, specific activity 14.33 mCi/mmol) was mixed with unlabeled dicamba acid (final specific activity of 4975 dpm/ g), reacted with aqueous dimethylamine, and formulated in water to prepare the test substance. The test material was applied at a nominal application rate of 0.5 lb ai/A (~0.67x the maximum seasonal application rate) to a 6.6 x 6.6 ft plot of sandy loam soil (79.0% sand, 13.0% silt, 8.0% clay, 1.0% organic matter, pH 6.9, cation exchange capacity 5.5 meq/100 g) that had been isolated from the surrounding soil by PVC edging. The details of method application (poured or sprayed) and soil incorporation for uniform distribution of test substance were not provided. A similar sized plot served as untreated control.

Half of the treated plot was planted with mustard seeds, turnip, and wheat at 32 days after treatment (DAT); the other half of the plot was planted to the same crops at 131 and 369-DAT. The test plots were fertilized before planting and the crops were irrigated to maintain adequate soil moisture. Information pertaining to daily precipitation, temperature, and irrigation was provided. The rotational crops were harvested as follows: mature mustard greens and turnip (root and tops) at 42, 58, and 54 days after the first, second, and third plantings, respectively; immature wheat at 42 and 54 days after the first and third plantings, respectively; and mature wheat at 275 days after the second planting. The turnip root and tops were composited from each sampling interval. The plant samples were frozen after collection and shipped on dry ice to Sandoz Crop Protection Corp. (Des Plaines, IL), where the samples were stored at <-10 C for an unspecified period, until analyzed.

Total Radioactive Residues (TRR)

The rotational crop samples were homogenized while frozen. The total radioactive residues in homogenized subsamples were determined by liquid scintillation spectrometry (LSS) following combustion. The limit of detection was 0.01 ppm. The TRR in samples of mustard greens, turnips, and wheat are presented in Table 2.

Table 2. Total radioactive residues (TRR) found in/on rotational crops grown in aged sandy loam soil that had been treated with [^{14}C]dicamba at ~0.67x.

Matrix	TRR (ppm, dicamba equivalents) [a]		
	32-Day Plantback	131-Day Plantback	369-Day Plantback
Mustard greens	0.213	<0.01	<0.01
Turnip [b]	0.0153	<0.01	<0.01
Wheat forage	0.0325	--	<0.01
Wheat grain	--	<0.01	--
Wheat straw	--	<0.01	--
Wheat chaff	--	<0.01	--

[a] Average of duplicate analyses. [b] Turnip root and tops were composited before analysis.

Extraction of Residues

The registrant provided descriptions of the procedures used for extraction and clean up of residues from plant commodities. Subsamples of homogenized matrices that contained >0.1 ppm TRR were extracted with 1 N HCl at 95 C for 1.5 hours. The acid hydrolysate was adjusted to pH ≥8 with 4 N KOH and then an aliquot was acidified to pH <1 with 6 N HCl. After centrifugation, the extract was partitioned twice with ethyl ether. The ether fractions were combined, concentrated, and saved for GC analysis. Quantitative raw data pertaining to TRR found in each fraction (HCl hydrolysate, ether extract, and non-extractable) of the rotational crop matrices were not provided.

Characterization and Identification of Residues

Residues in the ether extracts from 32-DAT mustard greens, turnip (root and top composite), and immature wheat were derivatized by butylation with N-butyl-N-nitro-N-nitrosoguanidine in butanol for 15 minutes. The derivatized residues were cleaned up using a silica gel column, eluted with 5-25% ethyl ether in pentane, and then analyzed for dicamba residues by GC/ECD. Radioactive metabolites were identified by comparison with the following unlabeled reference standards: dicamba acid, 5-hydroxy dicamba acid, and 3,6-dichlorosalicylic acid (DCSA). The limit of detection was 0.01 ppm for all the three reference standards. The registrant submitted details of the GC/ECD method (AM-0691B) and recoveries for dicamba acid (84-120%) and 5-hydroxy dicamba acid (74-110%) from control samples of plant commodities fortified with the analytes at 0.05-100.0 ppm; recovery data for DCSA were not provided.

Table 3 lists the reported qualitative results of the characterization and identification procedures. Sample calculations were provided, but raw data, material balance, and sample chromatograms for the GC/ECD analyses of rotational crop extracts were not submitted.

Storage Stability

The registrant did not submit any storage stability data to validate the results of this confined rotational crop study. The harvested samples of crop matrices were stored frozen at <-10 C. Dates of extraction and analysis were not provided. However, based on date of harvest (7/15/86 for 32-DAT samples) and reported date of completion of the study (12/28/88), it is estimated that plant samples from this rotational crop study may have been stored for up to 29 months.

Study Summary

The submitted confined rotational crop study is inadequate to satisfy the 165-1 guideline requirements because the test substance was applied at only 0.67x the maximum registered

Table 3. Distribution of total radioactive residues (TRR) in/on rotational crops grown in aged sandy loam soil treated with [^{14}C]dicamba at ~0.67x.

Fraction	% TRR	ppm	Characterization/Identification
32-DAT Mustard greens (0.213 ppm)			
HCl extract	NP [a]	NP	Partitioned with ethyl ether.
Ethyl ether	NP	NP	Dicamba, DCSA, and 5-OH dicamba were quantitated by GC/ECD at levels <0.01 ppm).
Non-extractable	NP	NP	N/A = Not analyzed.
32-DAT Turnip (0.0153 ppm)			
HCl extract	NP	NP	Partitioned with ethyl ether.
Ethyl ether	NP	NP	Dicamba, DCSA, and 5-OH dicamba were quantitated by GC/ECD at levels <0.01 ppm (LOD = 0.01 ppm).
Non-extractable	NP	NP	N/A
32-DAT Wheat forage (0.0325 ppm)			
HCl extract	NP	NP	Partitioned with ethyl ether.
Ethyl ether	NP	NP	Dicamba, DCSA, and 5-OH dicamba were quantitated by GC/ECD at levels <0.01 ppm (LOD = 0.01 ppm).
Non-extractable	NP	NP	N/A

[a] The %TRR and ppm in the soluble extracts and non-extractable residues were not provided.

dicamba label rate for annual crops. The possibility of obtaining rotational crop commodity samples with sufficient radioactive residues (e.g., at the 131- and 369-day plantback interval) may have been compromised as a result of the <1x application rate. Furthermore, the reported results of the characterization and identification of radioactive residues, using samples from the 32-day plantback interval, is inconclusive since details and quantitative raw data (e.g., material balance to account for the radioactivity in extractable and non-extractable fractions as well as sample chromatograms) were not provided. Upgrading the study by conducting further analyses on stored samples is not feasible because the study was initiated in 1986. A new confined rotational crop study must be conducted.

MASTER RECORD IDENTIFICATION NUMBERS

The citation for the MRID document referred to in this document is presented below.

41972001 Moore, P.A. and Butz, R. G. (1989) Confined Accumulation Studies of Dicamba on Rotational Crops After Spring Application. Lab Project No. 480065; Report No. 16. Unpublished study conducted and submitted by Sandoz Crop Protection Corporation (Des Plaines, IL). 125 p.

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Chemical:	**Dicamba**
PC Code:	**029801**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**02/15/1996**
File ID:	**DPD197629**
Accession Number:	**412-05-0098**

HED Records Reference Center
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